285. (New) The method of claim 270 wherein said monoclonal antibody has the immunoreaction characteristics of the monoclonal antibody LM609 having ATCC accession number HB 9537.

286. (New) The method of claim 270 wherein said monoclonal antibody is humanized.--

REMARKS

Consideration of this application in view of the amendments above and the discussion below is respectfully requested.

Claims 17-170 are canceled. New claims 171-286 have been added. The amendments made herein are without prejudice to Applicants' right to pursue the now canceled subject matter in a timely-filed continuation, divisional or continuation-in-part application. In addition, the amendments are expressly not to be construed as an abandonment of the subject matter or an acquiescence to any grounds for rejection that may be outstanding in this matter. Thus, claims 171-286 are pending. The amendments to the specification are to provide an amended title, and to correct obvious typographical errors. Appendix I provides the marked-up version of the amendments to the specification.

Applicants believe that no new matter has been introduced by the amendments made herein.

I. The Amendments

Support for adding the new claims is found in the canceled claims. Additionally, new claims 176, 192, 209, 227, 243, 257 and 274 have support at page 22, lines 22-26; new claims 179, 181-183, 195, 197-199, 212, 214-216, 230, 232-234, 246, 248-250, 260, 262-264, 277, and 279-281 have support at page 19, lines 1-3; claim 189 has support at page 14, lines 8-11 and claims 252 and 270 have support at page 16, lines

13-27.

With regard to the comments, objections and rejections presented in the Action by the Examiner, Applicants' response continues below.

II. The Restriction Requirement

In the Response to Restriction Requirement mailed January 29, 2001, Applicants elected, without traverse, Group I that includes claims 17-23, 28-42, 64-84, 144-150 and 155-170. The Examiner has requested that Applicants now clarify the distinction between Groups I, III and IV, as previously set forth in PTO Restriction Requirement (Paper No. 12). The new claims containing the elected species correspond to the claims as recited in Group I. In view of the presentation of new claims reciting the elected species, Applicants believe that any clarification of the Examiner imposed restriction is unnecessary at this time.

III. Sequence Listing

The Examiner has requested a replacement Sequence Listing that incorporates the amino acid residue sequence on page 4, line 31. Applicants have provided a replacement Sequence Listing, both on electronic and paper versions, along with a Response directing its entry.

IV. Priority and Related Amendment

The Examiner has requested that the specification be amended to recite prior applications and related priority information. Applicants have provided the enclosed Supplemental Application Data Statement (ADS) in compliance with 37 CFR §1.76. The ADS provides the priority information that need not otherwise be made part of the specification. The present application was filed before November 29, 2000, the effective date of compliance with 37 CFR §1.78(a)(2) in which the claim for priority must

be made within the later of four months from the filing date of the present application or sixteen months from the filing date of the prior application. Therefore, no petition is required to present the claim for priority in the ADS. Applicants request that the priority claim as recited in the ADS be entered.

V. Objections to the Specification

The Examiner requested that the specification be amended to reflect reference to prior applications. The submitted ADS provides the requested reference and the priority claim as discussed above.

The Examiner further requested that the title be amended to be more descriptive of the invention to which the claims are directed. Applicants provide the amended title in the Amendment section.

The Examiner has indicated that the drawing and photographs submitted with the application fail to comply with 37 C.F.R .§1.84. Applicants will provide the formal compliant drawings and photographs in a separate mailing.

The Examiner has requested that Applicants review and provide necessary amendments to the specification to correct obvious errors. Applicants have reviewed the specification and have provided the relevant amendments.

In view of the foregoing, Applicants request that the objections to the specification be withdrawn.

VI. Supplemental Information Disclosure Statement

Applicants have enclosed in the present response a supplemental Information Disclosure Statement and request its entry.

VII. Compliance with 35 U.S.C. §112 Deposit Requirements

The Examiner has correctly noted that the LM609 antibody having ATCC Accession Number HB9537 was first recited in the parent application, U.S. Patent No.

5,752,230, to which the present application claims priority. The Examiner has indicated that the claims 37, 79 and 164 reciting the antibody are considered in compliance with the deposit requirements. Applicants have canceled those claims. New claims 187, 203, 220, 238, 240, 268, and 285 recite the LM609 antibody and, thus, are likewise in compliance with the deposit requirements.

VIII. Rejections under 35 U.S.C. §102(a)

Claims 17-20, 22, 28, 29, 31-38, 64-66, 68, 70, 71, 73-80, 144-147, 155-165 and 170

Claims 17-20, 22, 28, 29, 31-38, 64-66, 68, 70, 71, 73-80, 144-147, 155-165 and 170 are rejected under 35 U.S.C. §102(a) as being anticipated by Kim (WO 93/20229).

Applicants have canceled the rejected claims without acquiescing to the basis for their rejection and have not abandoned Applicants' right to pursue the canceled subject matter in a timely filed continuing application.

In view of the foregoing, Applicants contend that the rejection for anticipation by Kim is no longer relevant. Applicants further note that the new claims all incorporate limitations of claims that the Examiner did not reject under Section 102 and, thus, were deemed novel by the Examiner. Accordingly, Applicants submit that the claims added herein should likewise be considered novel by the Examiner.

IX. Rejections under 35 U.S.C. §102(b)

Claims 17-20, 22, 28, 29, 31-35, 37, 64-66, 68, 70, 71, 73-77, 79, 144-147, 155-162, 164 and 170

Claims 17-20, 22, 28, 29, 31-35, 37, 64-66, 68, 70, 71, 73-77, 79, 144-147, 155-162, 164 and 170 are rejected under 35 U.S.C. §102(a) as being anticipated by Cheresh (WO 89/05155).

Applicants have canceled the rejected claims without acquiescing to the basis for their rejection and have not abandoned Applicants' right to pursue the canceled subject

matter in a timely filed continuing application. Applicants have submitted new claims for consideration.

In view of the foregoing, Applicants contend that the rejection for anticipation by Cheresh is no longer relevant. Applicants further note that the new claims all incorporate limitations of claims that the Examiner did not reject under Section 102 and, thus, were deemed novel by the Examiner. Accordingly, Applicants submit that the claims added herein should likewise be considered novel by the Examiner.

X. Rejection under 35 U.S.C. §103(a)

1. Claims 17-23, 28-38, 64-80, 144-150, 155-165 and 170

Claims 17-23, 28-38, 64-80, 144-150, 155-165 and 170 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kim (WO 93/20229) and/or Cheresh (WO 89/05155) in view of Nicosia et al. (Am. J. Pathol., 138:829-833, 1991), Nip et al. (J. Clin. Invest., 90:1406-1413, 1992), Folkman et al., (Seminars in Cancer Biology, 3:89-96, 1992), and art known procedures of treating cancers of interest at the time the invention was made.

Applicants have canceled the rejected claims without acquiescing to the basis for their rejection and have not abandoned Applicants' right to pursue the canceled subject matter in a timely filed continuing application. Applicants have submitted new claims for consideration.

All of the new claims specify, *inter alia*, either that the type of tissue growth or metastasis being inhibited is bladder, breast, colon or lung tumor tissue or angiofibroma, retrolental fibroplasia, hemangioma or Kaposi's Sarcoma tissue (claims 171-251) or that the human being administered had previously been treated for a solid tumor (claims 252-286). Moreover, all the claims have been limited to monoclonal antibodies immunospecific for $\alpha_v\beta_3$ to conform to Applicants' species election. Neither of the two primary references, Kim or Cheresh, teach administration of antibodies immunospecific for $\alpha_v\beta_3$ to the tissue types specified in claims 171-251 or teach such

administration to humans who have previously been otherwise treated for the tumor. The cited secondary references do not cure the defect of the primary references. Nip is the only one of the cited secondary references that teaches the use of an antibody immunospecific for $\alpha_v\beta_3$ and, as such, is the only one of the cited secondary references even remotely relevant to the newly added claims. Nip only teaches that an antibody immunospecific for $\alpha_v\beta_3$ can block adhesion of melanoma cells to lymph node tissue *in vitro* and in no way suggests the claimed invention. Without even a suggestion of the invention, Nip certainly does not provide an expectation of success. Because there is no suggestion of the invention, much less an expectation of success, the cited references do not render the claimed invention obvious. Accordingly, Applicants submit that the claims added herein are novel and nonobvious over the prior art.

2. Claims 17-23, 28-38, 64-80, 144-150, 155-165 and 170

Claims 17-23, 28-38, 64-80, 144-150, 155-165 and 170 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kim (WO 93/20229) and/or Cheresh (WO 89/05155) in view of art known procedures of treating cancers of interest at the time the invention was made as applied to claims 17-23, 28-38, 64-80, 144-150, 155-165 and 170 and further in view of Nicosia et al. (Am. J. Pathol., 138:829-833, 1991), Nip et al. (J. Clin. Invest., 90:1406-1413, 1992), and Folkman et al., (Seminars in Cancer Biology, 3:89-96, 1992).

Applicants have canceled the rejected claims without acquiescing to the basis for their rejection and have not abandoned Applicants' right to pursue the canceled subject matter in a timely filed continuing application. Applicants have submitted new claims for consideration.

All of the new claims specify, *inter alia*, either that the type of tissue growth or metastasis being inhibited is bladder, breast, colon or lung tumor tissue or angiofibroma, retrolental fibroplasia, hemangioma or Kaposi's Sarcoma tissue (claims 171-251) or that the human being administered had previously been treated for a solid

tumor (claims 252-286). Moreover, all the claims have been limited to monoclonal antibodies immunospecific for $\alpha_v\beta_3$ to conform to Applicants' species election. Neither of the two primary references, Kim or Cheresh, teach administration of antibodies immunospecific for $\alpha_v\beta_3$ to the tissue types specified in claims 171-251 or teach such administration to humans who have previously been otherwise treated for the tumor. The cited secondary references do not cure the defect of the primary references. Nip is the only one of the cited secondary references that teaches the use of an antibody immunospecific for $\alpha_v\beta_3$ and, as such, is the only one of the cited secondary references even remotely relevant to the newly added claims. Nip only teaches that an antibody immunospecific for $\alpha_v\beta_3$ can block adhesion of melanoma cells to lymph node tissue *in vitro* and in no way suggests the claimed invention. Without even a suggestion of the invention, Nip certainly does not provide an expectation of success. Because there is no suggestion of the invention, much less an expectation of success, the cited references do not render the claimed invention obvious. Accordingly, Applicants submit that the claims added herein are novel and nonobvious over the prior art.

XI. Summary

Applicants believe that a complete response is provided in the foregoing amendments and remarks to each issue and grounds for rejection and objection raised by the Examiner. Applicants submit that patentable subject matter exists with regard to the pending claims and therefore respectfully requests favorable action and entry of the presents Amendments and Response. The application is now believed to be in proper condition for allowance and early notification of allowance is earnestly solicited. The

Examiner is invited to telephone the undersigned if it would be deemed helpful to advance the application.

Respectfully submitted,

October 10, 2001
Date

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